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Design of Biomedical and Biofunctional Polymers by Use of Living/Controlled Polymerizations and "Click" Chemistry

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The lecture will address recent research activities aiming at developing novel biomacromolecular materials with unsurpassed properties by use of the proper synthetic tools where various "click" chemistry approaches play a key prominent role. Two entirely different themes will be elaborated with first application of orthogonal "clicking" employing both the copper catalyzed alkyne azide 1,3-cycloaddition (CuAAC) and thiol-ene "click" and lastly "electroclicking" onto a conducting polymer surface.

In the first part the classical medical material workhorse, poly(ε-caprolactone) (PCL), has been employed as a viable scaffold for design of several novel materials with intriguing, potentially therapeutic and biological properties. Living ROP strategies have afforded telechelic PCLs that can be equipped with various functional groups including "clickable" moieties or turned into macromonomers applicable for ATRP resulting in multi-component materials. In the first approach gold nanoparticles are protected with a polymeric shell that may combine ablative therapy and site-specific drug delivery in bladder cancer therapy.[1] This may be accomplished by tailoring the surface properties and the size of the gold clusters. The former may be addressed by devising polymeric ligands with desirable features and functional groups. Thus the preparation of the PCL-*b*-PAA corona will be outlined. The second effort is the ligation of biologically active moieties to the termini of the hydrophobic PCL chain to afford the amphiphilic linear-dendritic macromolecule that comprises rod-like, coil-like, and dendritic fragments. The facile route to linear-dendritic cholesteryl-*b*-PCL-*b*-(L-lysine)$_{G2}$ by azide-alkyne and thiol-ene "click" reactions will be elucidated.[2] Here the driving motivation was to contrive a robust, facile, and effective synthetic strategy. Thirdly, the preparation of PCL-based miktoarm core-crosslinked amphiphilic star copolymers with hydrophobic interior, charged hydrophilic surface, and targeting motifs are elaborated.[3] Such nanoscopic core-shell type architectures are envisioned to be excellent candidates as drug delivery devices owing to the enhanced stability in biological fluids. Moreover, they may permit site-specific delivery of their potential cargo due to the presence of biologically active moieties such as estradiol and L-lysine on the peripheries.

In the second part novel azide containing, conductive (co)polymers based on poly(3,4-(1-azidomethylethylenedioxy-thiophene)) (PEDOT-N_3) have been prepared.[4] This enables introduction of new functionalities onto the conductive polymer. The CuAAC on the insoluble conductive polymer was optimized using a fluorescent alkyne. The original relative slow "click" reaction on the order of tens of hours in order to reach full conversion can be performed in only a few minutes by use of microwaves in a simple kitchen microwave oven.[5] In a further development, it is demonstrated that the reaction can be localized spatially and selectively on either of a pair of interdigitated electrodes.[6] The conducting polymer microelectrodes can electrochemically generate the catalyst required for their own functionalization by "click" chemistry with high spatial resolution. Through control of the applied electrode potentials the electrodes are selectively functionalized in sequence as demonstrated by use of two alkyne-modified fluorophores. For this method we have introduced the term "electroclick". In the most recent development complex one- or two-dimentional concentration gradients of alkynated molecules are produced locally on the PEDOT-N_3 by stenciled "electroclick" chemistry.[7] A stencil on the counter electrode defines the shape and multiplicity of the gradient(s) on the conducting polymer substrate, whereas the specific reaction conditions control gradient steepness and the maximum concentration deposited. Biologically active ligands including cell binding peptides are patterned in gradients by this method without losing their biological function or the conductivity of the polymer.

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